AMENDMENTS TO THE CLAIMS

1-107. (Canceled)

108. (Currently amended) A method for determining whether a first trait T_1 is causal for, reactive to, or independent of a second trait T_2 in a plurality of organisms of a species, the method comprising:

(A) identifying one or more loci in the genome of said species, wherein each locus *Q* of said one or more loci is a site of colocalization for (i) a respective quantitative trait locus (QTL_1) that is genetically linked to a variation in the first trait T_1 across the plurality of organisms and (ii) a respective quantitative trait locus (QTL_2) that is genetically linked to a variation in the second trait T_2 across said plurality of organisms; and

(B) determining whether said first trait T_1, is causal for, reactive to, or independent of, said second trait T_2, comprising testing, for each respective locus *Q* of said one or more loci identified in step (A), whether (i) a genetic variation *Q** of said respective locus *Q* across said plurality of organisms and (ii) said variation in said second trait T_2 across said plurality of organisms are correlated conditional on said variation in said first trait T_1 across said plurality of organisms,

wherein, when the genetic variation of (i) one or more loci *Q* tested in (B), and (ii) said variation in said second trait T_2 across said plurality of organisms are correlated conditional on said variation in said first trait T_1 across said plurality of organisms, said first trait T_1 is determined to be causal for, and not reactive or independent of, said second trait T_2, wherein step (B) is performed by a suitably programmed computer.

109. (Previously presented) The method of claim 108, the method further comprising, prior to said identifying, a step of determining a respective QTL_1 at a locus *Q* of said one or

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more loci using a first quantitative trait locus (QTL) analysis, wherein said first QTL analysis uses a plurality of quantitative measurements of said first trait, and wherein each quantitative measurement in said plurality of quantitative measurements of said first trait is obtained from an organism in said plurality of organisms.

110. (Previously presented) The method of claim 109, the method further comprising a step of determining a respective QTL_2 at said locus *Q* using a second QTL analysis, wherein said second QTL analysis uses a plurality of quantitative measurements of said second trait, and wherein each quantitative measurement in said plurality of quantitative measurements of said second trait is obtained from an organism in said plurality of organisms.

111. (Original) The method of claim 108, wherein said respective QTL_1 and said respective QTL_2 are deemed to be colocalized at a locus *Q* of said one or more loci when said respective QTL_1 and said respective QTL_2 are within 3 cM of the locus *Q*.

112. (Original) The method of claim 108, wherein said respective QTL_1 and said respective QTL_2 are deemed to be colocalized at a locus *Q* of said one or more loci when said respective QTL_1 and said respective QTL_2 are within 1 cM of the locus *Q*.

113. (Original) The method of claim 108 wherein said plurality of organisms is derived from a predetermined set of individuals.

114. (Original) The method of claim 108 wherein said plurality of organisms is derived from a predetermined set of strains.

115. (Original) The method of claim 114 wherein said set of strains is between 2 strains and 100 strains.

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116. (Original) The method of claim 114 wherein said set of strains is between 5 strains and 500 strains.

117. (Original) The method of claim 114 wherein said set of strains is more than five strains.

118. (Original) The method of claim 114 wherein said set of strains is less than 1000 strains.

119. (Currently amended) The method of claim 114 wherein said set of strains is diverse with respect to a complex phenotype ~~associated~~ having a correlated occurrence across a population with a human disease.

120. (Currently amended) The method of claim 114 wherein said set of strains is between 2 strains and 10 strains that, collectively, are diverse with respect to a complex phenotype ~~associated~~ having a correlated occurrence across a population with a human disease.

121. (Original) The method of claim 120 wherein said human disease is obesity, diabetes, atherosclerosis, metabolic syndrome, depression, anxiety, osteoporosis, bone development, asthma, or chronic obstructive pulmonary disease.

122. (Original) The method of claim 108 wherein said plurality of organisms is derived from crossing a predetermined set of strains.

123. (Original) The method of claim 122 wherein said plurality of organisms is an F_2 intercross, a backcross, or an F_2 random mating.

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124. (Original) The method of claim 108 wherein the plurality of organisms is more than 1,000 organisms.

125. (Original) The method of claim 108 wherein the plurality of organism is between 100 organisms and 100,000 organisms.

126. (Original) The method of claim 108 wherein the plurality of organisms is less than 500,000 organisms.

127. (Original) The method of claim 108 wherein the plurality of organisms is between 5,000 and 25,000 organisms.

128. (Original) The method of claim 109, wherein

said first trait is abundance levels of a first cellular constituent and each quantitative measurement of said first trait is an abundance level of said first cellular constituent in an organism in said plurality of organisms; and

said second trait is abundance levels of a second cellular constituent and each quantitative measurement of said second trait is an abundance level of said second cellular constituent in an organism in said plurality of organisms.

129. (Previously presented) The method of claim 128 wherein each said abundance level of said first cellular constituent is normalized and each said abundance level of said second cellular constituent is normalized.

130. (Original) The method of claim 128 wherein

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each said abundance level of said first cellular constituent is determined by measuring an amount of said first cellular constituent in one or more cells from an organism in said plurality of organisms; and

each said abundance level of said second cellular constituent is determined by measuring an amount of said second cellular constituent in one or more cells from an organism in said plurality of organisms.

131. (Original) The method of claim 128, wherein

each said amount of said first cellular constituent comprises an abundance of a first RNA in said one or more cells of said organism in said plurality of organisms; and

each said amount of said second cellular constituent comprises an abundance of a second RNA in said one or more cells of said organism in said plurality of organisms.

132. (Previously presented) The method of claim 131, wherein

said abundance of said first RNA is measured by contacting a gene transcript array with said first RNA from said one or more cells of said organism, or with nucleic acid derived from said first RNA, wherein said gene transcript array comprises a positionally addressable surface with attached nucleic acids or nucleic acid mimics, wherein said nucleic acids or nucleic acid mimics are capable of hybridizing with said first RNA, or with nucleic acid derived from said first RNA; and

said abundance of said second RNA is measured by contacting a gene transcript array with said second RNA from said one or more cells of said organism, or with nucleic acid derived from said second RNA, wherein said gene transcript array comprises a positionally addressable surface with attached nucleic acids or nucleic acid mimics, wherein said nucleic acids or nucleic

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acid mimics are capable of hybridizing with said second RNA, or with nucleic acid derived from said second RNA.

133. (Original) The method of claim 109, wherein said first QTL analysis comprises:

(i) testing for linkage between (a) the genotype of said plurality of organisms at a position in the genome of said species and (b) said plurality of quantitative measurements of said first trait;

(ii) advancing the position in said genome by an amount; and

(iii) repeating steps (i) and (ii) until all or a portion of the genome of said species has been tested.

134. (Original) The method of claim 110, wherein said second QTL analysis comprises:

(i) testing for linkage between (a) the genotype of said plurality of organisms at a position in the genome of said species and (b) said plurality of quantitative measurements of said second trait;

(ii) advancing the position in said genome by an amount; and

(iii) repeating steps (i) and (ii) until all or a portion of the genome of said species has been tested.

135-136. (Canceled)

137. (Original) The method of claim 133 or 134, wherein said testing comprises performing linkage analysis or association analysis.

138. (Original) The method of claim 137, wherein said linkage analysis or association analysis generates a statistical score for said position in the genome of said species.

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139. (Original) The method of claim 138, wherein said testing is linkage analysis and said statistical score is a logarithm of the odds (lod) score.

140-141. (Canceled)

142. (Original) The method of claim 109, wherein said respective QTL_1 is represented by a lod score that is greater than 4.0.

143. (Original) The method of claim 110, wherein said respective QTL_2 is represented by a lod score that is greater than 4.0.

144. (Original) The method of claim 109 wherein each quantitative measurement in said plurality of quantitative measurements of said first trait is

an amount or a concentration of a first cellular constituent in one or more tissues of an organism in said plurality of organisms,

a cellular constituent activity level of said first cellular constituent in one or more tissues of an organism in said plurality of organisms, or

a state of cellular constituent modification of said first cellular constituent in one or more tissues of an organism in said plurality of organisms.

145. (Original) The method of claim 110 wherein each quantitative measurement in said plurality of quantitative measurements of said second trait is

an amount or a concentration of a second cellular constituent in one or more tissues of an organism in said plurality of organisms,

a cellular constituent activity level of said second cellular constituent in one or more tissues of an organism in said plurality of organisms, or

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a state of cellular constituent modification of said second cellular constituent in one or more tissues of an organism in said plurality of organisms.

146. (Original) The method of claim 108, wherein said plurality of organisms is human.

147. (Original) The method of claim 109, wherein said respective QTL_1 and said respective QTL_2 are deemed to colocalize at a locus Q of said one or more loci when said respective QTL_1 and said respective QTL_2 are within 40 cM of the locus Q.

148. (Original) The method of claim 109, wherein said respective QTL_1 and said respective QTL_2 are deemed to colocalize at a locus Q of said one or more loci when said respective QTL_1 and said respective QTL_2 are within 10 cM of the locus Q.

149. (Original) The method of claim 108 wherein said one or more loci consist of at least two loci.

150. (Original) The method of claim 108, wherein said respective QTL_1 and said respective QTL_2 colocalize at a locus Q of said one or more loci when said respective QTL_1 and said respective QTL_2 satisfy a pleiotropy test and wherein failure of the pleiotropy test indicates that (i) the respective QTL_1 and the respective QTL_2 are two closely linked QTL, (ii) step (B) is not performed, and (iii) said first trait T_1 is not determined to be causal for said second trait T_2.

151. (Original) The method of claim 150 wherein said pleiotropy test comprises comparing a model for a null hypothesis, indicating that said respective QTL_1 and said respective QTL_2 colocalize as a QTL, to a model for an alternative hypothesis, indicating that said QTL_1 and said respective QTL_2 are two closely linked QTL.

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152. (Currently amended) The method of claim 151 wherein said model for said null hypothesis is:

$$\begin{pmatrix}\gamma_1\\ \gamma_2\end{pmatrix}=\begin{pmatrix}\mu_1\\ \mu_2\end{pmatrix}=\begin{pmatrix}\beta_1\\ \beta_2\end{pmatrix}N+\begin{pmatrix}\varepsilon_1\\ \varepsilon_2\end{pmatrix}$$

wherein

N is a categorical random variable indicating the genotype at locus Q across said plurality of organisms;

$\begin{pmatrix}\varepsilon_1\\ \varepsilon_2\end{pmatrix}$ is distributed as a bivariate normal random variable with mean $\begin{pmatrix}0\\ 0\end{pmatrix}$ and covariance matrix $\begin{pmatrix}\sigma_1^2 & \sigma_1\sigma_2\\ \sigma_2\sigma_1 & \sigma_2^2\end{pmatrix}$; and

μ_i and β_i are model parameters.

153. (Original) The method of claim 151 wherein said model for said alternative hypothesis is:

$$\begin{pmatrix}\gamma_1\\ \gamma_2\end{pmatrix}=\begin{pmatrix}\mu_1\\ \mu_2\end{pmatrix}=\begin{pmatrix}\beta_1 & \beta_2\\ \beta_3 & \beta_4\end{pmatrix}\begin{pmatrix}N_1\\ N_2\end{pmatrix}+\begin{pmatrix}\varepsilon_1\\ \varepsilon_2\end{pmatrix}$$

wherein

N_1 and N_2 are categorical random variables indicating the genotype at locus Q across said plurality of organisms;

$\begin{pmatrix}\varepsilon_1\\ \varepsilon_2\end{pmatrix}$ is distributed as a bivariate normal random variable with mean $\begin{pmatrix}0\\ 0\end{pmatrix}$ and covariance matrix $\begin{pmatrix}\sigma_1^2 & \sigma_1\sigma_2\\ \sigma_2\sigma_1 & \sigma_2^2\end{pmatrix}$; and

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μ_i and β_i are model parameters.

154. (Previously presented) The method of claim 152 wherein said model for said alternative hypothesis is:

$$\begin{pmatrix}\gamma_1\\ \gamma_2\end{pmatrix}=\begin{pmatrix}\mu_1\\ \mu_2\end{pmatrix}+\begin{pmatrix}\beta_1 & \beta_2\\ \beta_3 & \beta_4\end{pmatrix}\begin{pmatrix}N_1\\ N_2\end{pmatrix}+\begin{pmatrix}\varepsilon_1\\ \varepsilon_2\end{pmatrix}$$

wherein

Q_1 and Q_2 are categorical random variables indicating the genotype at locus Q across said plurality of organisms;

$\begin{pmatrix}\varepsilon_1\\ \varepsilon_2\end{pmatrix}$ is distributed as a bivariate normal random variable with mean $\begin{pmatrix}0\\ 0\end{pmatrix}$ and covariance matrix $\begin{pmatrix}\sigma_1^2 & \sigma_1\sigma_2\\ \sigma_2\sigma_1 & \sigma_2^2\end{pmatrix}$;

μ_i and β_i are model parameters; and one of the conditions (i) through (iv) is valid:

(i) $\beta_1 \neq 0$, $\beta_4 \neq 0$, $\beta_2 = 0$, and $\beta_3 = 0$;

(ii) $\beta_1 \neq 0$, $\beta_4 \neq 0$, $\beta_2 \neq 0$, and $\beta_3 = 0$;

(iii) $\beta_1 \neq 0$, $\beta_4 \neq 0$, $\beta_2 = 0$, and $\beta_3 \neq 0$; and

(iv) $\beta_1 \neq 0$, $\beta_4 \neq 0$, $\beta_2 \neq 0$, and $\beta_3 \neq 0$.

155. (Original) The method of claim 151 wherein said comparing comprises:

obtaining a first maximum likelihood estimate for the model for the null hypothesis by maximizing the loglikelihood for the model for the null hypothesis with respect to model parameters;

obtaining a second maximum likelihood estimate for the model for the alternative hypothesis by maximizing the loglikelihood for the model for the alternative hypothesis with respect to model parameters; and

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forming a likelihood ratio test statistic between the first maximum likelihood estimate and said second maximum likelihood estimate to determine whether the model for the alternative hypothesis provides for a statistically significant better fit to the data than the model for the null hypothesis.

156. (Previously presented) The method of claim 108 wherein said testing comprises considering a null test for causality having the relationship:

$$P(T_2, Q^* | T_1) = P(T_2 | G) P(Q^* | T_1),$$

wherein

each function P is a probability density function;

T_2 is the variation of the second trait across said plurality of organisms;

Q^* is a genotype random variable for a locus Q of said one or more loci across said plurality of organisms; and

T_1 is the variation of the first trait across said plurality of organisms.

157. (Original) The method of claim 156 wherein said testing comprises comparing said null test for causality, indicating that said first trait T_1 is causal for said second trait T_2, to an alternative hypothesis, indicating that T_2 and Q are dependent given T_1.

158. (Original) The method of claim 157 wherein said testing comprises optimizing the log likelihood ratio of said null hypothesis and said alternative hypothesis using maximum likelihood analysis.

159. (Currently amended) A computer program product for use in conjunction with a computer system, the computer program product comprising a computer readable storage

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medium and a computer program mechanism embedded therein, the computer program mechanism comprising:

a T_1/T_2 overlap module that comprises instructions for identifying one or more loci in the genome of a species, wherein each locus *Q* of said one or more loci is a site of colocalization for (i) a respective quantitative trait locus (QTL_1) that is genetically linked to a variation in a first trait T_1 across a plurality of organisms in said species and (ii) a respective quantitative trait locus (QTL_2) that is genetically linked to a variation in a second trait T_2 across said plurality of organisms; and

a causality test module, for determining whether said first trait T_1 is causal for reactive to, or independent of said second trait T_2 that comprises instructions for testing, for one or more locus *Q* of said one or more loci, whether (i) a genotype random variable *Q** of the respective locus *Q* across the plurality of organisms and (ii) said variation in the second trait T_2 across the plurality of organisms are correlated conditional on the variation in said first trait T_1 across the plurality of organisms.

160. (Currently amended) A computer system comprising:

a central processing unit;

a memory, coupled to the central processing unit, the memory storing an Q_1/Q_2 overlap module and a causality test module; wherein

the T_1/T_2 overlap module comprises instructions for identifying one or more loci in the genome of a species, wherein each locus *Q* of said one or more loci is a site of colocalization for (i) a respective quantitative trait locus (QTL_1) that is genetically linked to a variation in the first trait T_1 across a plurality of organisms of said species and (ii) a respective quantitative trait locus (QTL_2) that is genetically linked to a variation in the second trait T_2 across said plurality of organisms; and

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a causality test module for determining whether said first trait T_1 is causal for, reactive to, or independent of, said second trait T_2 that comprises instructions for testing, for one or more loci Q in the at least one locus, whether (i) a genotype random variable $Q*$ for the respective locus Q across the plurality of organisms and (ii) said variation in said second trait T_2 across said plurality of organisms are correlated conditional on the variation in the first trait T_1 across said plurality of organisms.

161-210. (Canceled)

211. (Currently amended) A method for determining whether a first trait T_1 is causal for, reactive to, or independent of a second trait T_2 in a plurality of organisms of a species, the method comprising:

(A) identifying a locus Q in the genome of said species that is a site of colocalization for (i) a quantitative trait locus (QTL_1) that is genetically linked to a variation in the first trait T_1 across all or a portion of the plurality of organisms and (ii) a quantitative trait locus (QTL_2) that is genetically linked to a variation in the second trait T_2 across all or a portion of said plurality of organisms;

(B) quantifying a first coefficient of determination between (i) a genetic variation $Q*$ of said locus Q across all or a portion of said plurality of organisms and (ii) said variation in said first trait T_1 across all or a portion of said plurality of organisms; and

(C) quantifying a second coefficient of determination between (i) said genetic variation $Q*$ of said locus Q across all or a portion of said plurality of ~~organsisms~~ organisms and (ii) said variation in said first trait T_1 across all or a portion of said plurality of ~~organsims~~ organisms, after conditioning on said variation in said second trait T_2 across all or a portion of said plurality of organisms, wherein

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said first trait T_1 is deemed to be causal for, and not reactive to, or independent of, said second trait T_2 when said first coefficient of determination is other than zero and said second coefficient of determination cannot be distinguished from zero, wherein at least one of steps (A) or (B) is performed by a suitably programmed computer.

212. (Previously presented) The method of claim 211 wherein said first trait T_1 is deemed to be causal for said second trait T_2 when said first coefficient of determination is greater than a predetermined threshold amount.

213. (Original) The method of claim 212 wherein said predetermined threshold amount is 0.03.

214. (Original) The method of claim 212 wherein said predetermined threshold amount is 0.10.

215. (Original) The method of claim 211, wherein said QTL_1 and said QTL_2 are deemed to colocalize at said locus *Q* when said QTL_1 and said QTL_2 are within 3 cM of the locus *Q*.

216. (Original) The method of claim 211, wherein said QTL_1 and said QTL_2 are deemed to colocalize at said locus *Q* when said QTL_1 and said QTL_2 are within 1 cM of the locus *Q*.

217. (Original) The method of claim 211 wherein the plurality of organisms is between 100 organisms and 100,000 organisms.

218. (Original) The method of claim 211 wherein the plurality of organisms is less than 500,000 organisms.

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219. (Original) The method of claim 211 wherein the plurality of organisms is between 5,000 and 25,000 organisms.

220. (Original) The method of claim 211 wherein said plurality of organisms is human.

221. (Original) The method of claim 211, wherein said first trait T_1 is a complex trait.

222. (Original) The method of claim 221, wherein said complex trait is characterized by an allele that exhibits incomplete penetrance in said species.

223. (Previously presented) The method of claim 221, wherein said complex trait is a disease that is contracted by at least one organism in said plurality of organisms, and wherein said organism inherits no predisposing allele to said disease.

224. (Original) The method of claim 221, wherein said complex trait arises when one or more of a plurality of different genes in the genome of said species is mutated.

225. (Original) The method of claim 221, wherein said complex trait requires the simultaneous presence of mutations in a plurality of genes in the genome of said species.

226. (Original) The method of claim 221, wherein said complex trait is a phenotype that does not exhibit Mendelian recessive or dominant inheritance attributable to a single gene locus.

227. (Original) The method of claim 221 wherein said complex trait is asthma, ataxia telangiectasia, bipolar disorder, cancer, common late-onset Alzheimer's disease, diabetes, heart disease, hereditary early-onset Alzheimer's disease, hereditary nonpolyposis colon cancer,

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hypertension, infection, maturity-onset diabetes of the young, mellitus, migraine, nonalcoholic fatty liver, nonalcoholic steatohepatitis, non-insulin-dependent diabetes mellitus, obesity, polycystic kidney disease, psoriases, schizophrenia, or xeroderma pigmentosum.

228. (Original) The method of claim 211 wherein said QTL_1 and said QTL_2 are deemed to colocalize at a locus *Q* of said one or more loci when said QTL_1 and said QTL_2 are within 40 cM of the locus *Q*.

229. (Original) The method of claim 211 wherein said QTL_1 and said QTL_2 are deemed to colocalize at a locus *Q* of said one or more loci when said QTL_1 and said QTL_2 are within 10 cM of the locus *Q*.

230. (Original) The method of claim 211 wherein said QTL_1 and said QTL_2 are deemed to colocalize at said locus *Q* when said QTL_1 and said QTL_2 satisfy a pleiotropy test and wherein failure of the pleiotropy test indicates that the QTL_1 and the QTL_2 are two closely linked QTL and said first trait T_1 is not determined to be causal for said second trait T_2.

231. (Original) The method of claim 230 wherein said pleiotropy test comprises comparing a model for a null hypothesis, indicating that said QTL_1 and said QTL_2 colocalize as a QTL, to a model for an alternative hypothesis, indicating that said QTL_1 and said QTL_2 are two closely linked QTL.

232. (Previously presented) The method of claim 231 wherein said model for said null hypothesis is:

$$\begin{pmatrix} y_1 \\ y_2 \end{pmatrix} = \begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix} + \begin{pmatrix} \beta_1 \\ \beta_2 \end{pmatrix} N + \begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \end{pmatrix}$$

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wherein

N is a categorical random variable indicating the genotype at locus Q across said plurality of organisms;

$\begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \end{pmatrix}$ is distributed as a bivariate normal random variable with mean $\begin{pmatrix} 0 \\ 0 \end{pmatrix}$ and covariance matrix $\begin{pmatrix} \sigma_1^2 & \sigma_1\sigma_2 \\ \sigma_2\sigma_1 & \sigma_2^2 \end{pmatrix}$; and

μ_i and β_i are model parameters.

233. (Original) The method of claim 231 wherein said model for said alternative hypothesis is:

$$\begin{pmatrix} \gamma_1 \\ \gamma_2 \end{pmatrix} = \begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix} + \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_3 & \beta_4 \end{pmatrix} \begin{pmatrix} N_1 \\ N_2 \end{pmatrix} + \begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \end{pmatrix}$$

wherein

N_1 and N_2 are categorical random variables indicating the genotype at locus Q across said plurality of organisms;

$\begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \end{pmatrix}$ is distributed as a bivariate normal random variable with mean $\begin{pmatrix} 0 \\ 0 \end{pmatrix}$ and covariance matrix $\begin{pmatrix} \sigma_1^2 & \sigma_1\sigma_2 \\ \sigma_2\sigma_1 & \sigma_2^2 \end{pmatrix}$; and

μ_i and β_i are model parameters.

234. (Original) The method of claim 231 wherein said model for said alternative hypothesis is:

$$\begin{pmatrix} \gamma_1 \\ \gamma_2 \end{pmatrix} = \begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix} + \begin{pmatrix} \beta_1 & \beta_2 \\ \beta_3 & \beta_4 \end{pmatrix} \begin{pmatrix} N_1 \\ N_2 \end{pmatrix} + \begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \end{pmatrix}$$

wherein

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Q_1 and Q_2 are categorical random variables indicating the genotype at locus Q across said plurality of organisms;

$\begin{pmatrix} \varepsilon_1 \\ \varepsilon_2 \end{pmatrix}$ is distributed as a bivariate normal random variable with mean $\begin{pmatrix} 0 \\ 0 \end{pmatrix}$ and covariance matrix $\begin{pmatrix} \sigma_1^2 & \sigma_1\sigma_2 \\ \sigma_2\sigma_1 & \sigma_2^2 \end{pmatrix}$; and

μ_i and β_i are model parameters; and one of the conditions (i) through (iv) is valid:

(i) $\beta_1 \neq 0$, $\beta_4 \neq 0$, $\beta_2 = 0$, and $\beta_3 = 0$;

(ii) $\beta_1 \neq 0$, $\beta_4 \neq 0$, $\beta_2 \neq 0$, and $\beta_3 = 0$;

(iii) $\beta_1 \neq 0$, $\beta_4 \neq 0$, $\beta_2 = 0$, and $\beta_3 \neq 0$; and

(iv) $\beta_1 \neq 0$, $\beta_4 \neq 0$, $\beta_2 \neq 0$, and $\beta_3 \neq 0$.

235. (Original) The method of claim 231 wherein said comparing comprises:

obtaining a first maximum likelihood estimate for the model for the null hypothesis by maximizing the loglikelihood for the model for the null hypothesis with respect to model parameters;

obtaining a second maximum likelihood estimate for the model for the alternative hypothesis by maximizing the loglikelihood for the model for the alternative hypothesis with respect to model parameters; and

forming a likelihood ratio test statistic between the first maximum likelihood estimate and said second maximum likelihood estimate to determine whether the model for the alternative hypothesis provides for a statistically significant better fit to the data than the model for the null hypothesis.

236-296. (Canceled)

297. (Currently amended) A computer program product for use in conjunction with a computer system, the computer program product comprising a computer readable storage

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medium and a computer program mechanism embedded therein, the computer program mechanism for determining whether a first trait T_1 is causal for, reactive to, or independent of, a second trait T_2 in a plurality of organisms of a species, the computer program mechanism comprising:

(A) instructions for identifying a locus *Q* in the genome of said species that is a site of colocalization for (i) a quantitative trait locus (QTL_1) that is genetically linked to a variation in the first trait T_1 across all or a portion of the plurality of organisms and (ii) a quantitative trait locus (QTL_2) that is genetically linked to a variation in the second trait T_2 across all or a portion of said plurality of organisms;

(B) instructions for quantifying a first coefficient of determination between (i) a genetic variation *Q** of said locus *Q* across all or a portion of said plurality of organisms and (ii) said variation in said first trait T_1 across all or a portion of said plurality of organisms; and

(C) instructions for quantifying a second coefficient of determination between (i) said genetic variation *Q** of said locus *Q* across all or a portion of said plurality of ~~organsisms~~ organisms and (ii) said variation in said first trait T_1 across all or a portion of said plurality of ~~organsims~~ organisms, after conditioning on said variation in said second trait T_2 across all or a portion of said plurality of organisms, wherein

said first trait T_1 is deemed to be causal for, and not reactive to or independent of, said second trait T_2 when said first coefficient of determination is other than zero and said second coefficient of determination cannot be distinguished from zero.

298. (Currently amended) A computer system comprising:

a central processing unit;

a memory, coupled to the central processing unit, the memory comprising:

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(A) instructions for identifying a locus *Q* in the genome of said species that is a site of colocalization for (i) a quantitative trait locus (QTL_1) that is genetically linked to a variation in the first trait T_1 across all or a portion of the plurality of organisms and (ii) a quantitative trait locus (QTL_2) that is genetically linked to a variation in the second trait T_2 across all or a portion of said plurality of organisms;

(B) instructions for quantifying a first coefficient of determination between (i) a genetic variation *Q** of said locus *Q* across all or a portion of said plurality of organisms and (ii) said variation in said first trait T_1 across all or a portion of said plurality of organisms; and

(C) instructions for quantifying a second coefficient of determination between (i) said genetic variation *Q** of said locus *Q* across all or a portion of said plurality of ~~organsisms~~ organisms and (ii) said variation in said first trait T_1 across all or a portion of said plurality of ~~organsims~~ organisms, after conditioning on said variation in said second trait T_2 across all or a portion of said plurality of organisms, wherein

said first trait T_1 is deemed to be causal for, and not reactive to or independent of, said second trait T_2 when said first coefficient of determination is other than zero and said second coefficient of determination cannot be distinguished from zero.

299. (Previously presented) The method of claim 108, wherein said second trait T_2 is a complex trait.

300. (Previously presented) The method of claim 299, wherein said complex trait is characterized by an allele that exhibits incomplete penetrance in said species.

301. (Previously presented) The method of claim 299, wherein said complex trait is a disease that is contracted by an organism in said plurality of organisms, and wherein said organism inherits no predisposing allele to said disease.

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302. (Previously presented) The method of claim 299, wherein said complex trait arises when any of a plurality of different genes in the genome of said species are mutated.

303. (Previously presented) The method of claim 299, wherein said complex trait requires the simultaneous presence of mutations in a plurality of genes in the genome of said species.

304. (Currently amended) The method of claim 299, wherein said complex trait ~~is associated~~ has a correlated occurrence across a population with a high frequency of disease-causing alleles in said species.

305. (Previously presented) The method of claim 299, wherein said complex trait is a phenotype that does not exhibit Mendelian recessive or dominant inheritance attributable to a single gene locus.

306. (Previously presented) The method of claim 299, wherein said complex trait is asthma, ataxia telangiectasia, bipolar disorder, cancer, common late-onset Alzheimer's disease, diabetes, heart disease, hereditary early-onset Alzheimer's disease, hereditary nonpolyposis colon cancer, hypertension, infection, maturity-onset diabetes of the young, mellitus, migraine, nonalcoholic fatty liver, nonalcoholic steatohepatitis, non-insulin-dependent diabetes mellitus, obesity, polycystic kidney disease, psoriases, schizophrenia, or xeroderma pigmentosum.

307. (Previously presented) The method of claim 109, wherein said first trait is abundance levels of a first cellular constituent and each quantitative measurement of said first trait is an abundance level of said first cellular constituent in an organism in said plurality of organisms.

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308. (Previously presented) The method of claim 211, wherein said second trait T_2 is a complex trait.

309. (Previously presented) The method of claim 308, wherein said complex trait is characterized by an allele that exhibits incomplete penetrance in said species.

310. (Previously presented) The method of claim 308, wherein said complex trait is a disease that is contracted by an organism in said plurality of organisms, and wherein said organism inherits no predisposing allele to said disease.

311. (Previously presented) The method of claim 308, wherein said complex trait arises when any of a plurality of different genes in the genome of said species are mutated.

312. (Previously presented) The method of claim 308, wherein said complex trait requires the simultaneous presence of mutations in a plurality of genes in the genome of said species.

313. (Previously presented) The method of claim 308, wherein said complex trait is associated with a high frequency of disease-causing alleles in said species.

314. (Previously presented) The method of claim 308, wherein said complex trait is a phenotype that does not exhibit Mendelian recessive or dominant inheritance attributable to a single gene locus.

315. (Previously presented) The method of claim 308, wherein said complex trait is asthma, ataxia telangiectasia, bipolar disorder, cancer, common late-onset Alzheimer's disease, diabetes, heart disease, hereditary early-onset Alzheimer's disease, hereditary nonpolyposis colon cancer, hypertension, infection, maturity-onset diabetes of the young, mellitus, migraine,

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nonalcoholic fatty liver, nonalcoholic steatohepatitis, non-insulin-dependent diabetes mellitus, obesity, polycystic kidney disease, psoriases, schizophrenia, or xeroderma pigmentosum.

316. (Previously presented) The method of claim 212, wherein said first trait is abundance levels of a first cellular constituent and each quantitative measurement of said first trait is an abundance level of said first cellular constituent in an organism in said plurality of organisms.

317. (Previously presented) The method of claim 108, wherein

the first trait T_1 is an abundance level of a cellular constituent;

each said respective quantitative trait locus (QTL_1) that is genetically linked to a variation in the first trait T_1 across the plurality of organisms is a respective abundance quantitative trait locus (eQTL) that is genetically linked to a variation in abundance levels of the cellular constituent across the plurality of organisms;

the second trait T_2 is a trait of interest **T** exhibited by one or more organisms in the plurality of organisms; and

each said respective quantitative trait locus (QTL_2) that is genetically linked to a variation in the second trait T_2 is a respective clinical quantitative trait locus (cQTL) that is genetically linked to a variation in the trait of interest **T** across the plurality of organisms.

318. (Previously presented) The method of claim 211, wherein

the first trait T_1 is an abundance level of a cellular constituent;

each said respective quantitative trait locus (QTL_1) that is genetically linked to a variation in the first trait T_1 across the plurality of organisms is a respective abundance quantitative trait locus (eQTL) that is genetically linked to a variation in abundance levels of the cellular constituent across the plurality of organisms;

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the second trait T_2 is a trait of interest **T** exhibited by one or more organisms in the plurality of organisms; and

each said respective quantitative trait locus (QTL_2) that is genetically linked to a variation in the second trait T_2 is a respective clinical quantitative trait locus (cQTL) that is genetically linked to a variation in the trait of interest **T** across the plurality of organisms.

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